## REMARKS

### In the Claims:

Claims 1, 3, 5-7, and 23-25 are pending. Claims 1, 3, and 24 are amended herein for purposes of increasing the clarity of the claims. Specifically, claims 1, 3, and 24 are amended to clarify that the plant to which the claimed method is applied is a plant that is used to prepare a standardized extract of that plant. No new matter is added by this amendment and support for the amendment may be found throughout the specification, including at paragraph 25 on page 7, and at paragraphs 32 and 33 on page 9.

Claims 1, 3, and 24 also are amended herein to clarify that a preparation of the plant is prepared for each maturation stage. No new matter is added by this amendment and support for the amendment may be found throughout the specification including at paragraph 19 on pages 4-5, and at paragraph 22 at page 5.

Claims 1, 3, and 24 further are amended herein to clarify that "an acceptable concentration of the marker compound" refers to a concentration of the marker compound that is acceptable for standardization of, for example, an *Echinacea* extract. No new matter is added by this amendment and support for the amendment may be found throughout the specification including at paragraph 17 on page 4, at Table I on page 6, at paragraph 24 on page 7, and at paragraph 32 on page 9.

Claims 3 and 24 are further amended to clarify that the plant referred to in these claims is an *Echinacea* plant and that it is the preparation of the *Echinacea* plant that induces an immune-stimulatory or translational product in the cell culture. No new matter is added by this amendment and support for the amendment may be found throughout the specification including at paragraphs 4 and 5 on page 2, and in original claims 3 and 24.

### 35 U.S.C. § 112, ¶ 1:

Claims 1, 3, 5-7, and 23-25 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. According to the Office action, "[i]t cannot be found in the instant specification as filed where

transcriptional products such as interleukins were quantified from *Echinacea* extracts." Page 3 of the Office action mailed 12/14/2006. The Office action requests that Applicants point out where such information may be found.

As an initial matter, Applicants respectfully note that the claims do not require that transcriptional products be quantified from *Echinacea* extracts, but rather require that such transcriptional products be isolated from cells exposed to *Echinacea* extracts. Independent claims 1, 3, and 24 are directed to "adding the preparations to monocyte (or macrophage) cell cultures." Paragraph 14 of the specification defines a "preparation" as "*Echinacea* plant products that result from the dehydrating and/or powdering of plant material or from the chemical extraction of plant material." Description of isolating transcriptional products such as interleukins from cells exposed to *Echinacea* extracts (*i.e.* a "preparation") may be found, for example, at paragraphs 15, 26-28, and 30 of the specification. Specifically, the preparations of *Echinacea* plant products referenced in paragraph 14 were prepared as described in paragraph 26 and tested in the gene induction assay described at paragraphs 26-31. At paragraphs 27 and 28, Applicants explain that THP-1 cells were exposed to *Echinacea* extracts (*i.e.* a "preparation") and following exposure to the extracts, mRNA expression "[l]evels of macrophage and monocyte-derived cytokines, including . . .interleukin (IL)-1 alpha . . . were measured at the transcription level." According to paragraph 30, "[t]he induction of immune cytokine mRNA . . . were measured by well-known methods of quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR)." The results of the gene induction assay are reported in Figure 1, as described in paragraph 15: "Figure 1 is a bar graph depicting the levels of mRNA for cytokines IL-1a, IL-1b, IL-6, IL-8, and IL-10 and levels of IFN-g, MIP-1 and TNF-a produced by THP-1 cells after treatment with extracts from *Echinacea* plants." Thus, Applicants respectfully submit that in these portions of the specification, Applicants disclose that transcription products, such as cytokines including interleukins-1a, 1b, 6, 8, and 10, were quantified from cells exposed to *Echinacea* extracts. Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

**35 U.S.C. § 112, ¶ 2:**

Claims 1, 3, 5-7, and 23-25 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office action alleges that the use of "acceptable" in claims 1 and 24 renders those claims indefinite because the specification does not provide any standard for ascertaining the requisite degree of acceptability.

Applicants respectfully disagree that "acceptable" is indefinite in claims 1 and 24. According to Section 2173.05(b) of the MPEP, "[t]he fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984)." Rather, the "[a]cceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification." MPEP § 2173.05(b). Applicants have herein amended the claims to clarify that the maturation stage is selected based on a concentration of marker compound that is acceptable for standardization of a plant extract. In the instant case, the specification provides the appropriate standard for ascertaining the requisite degree of acceptability for standardization. Specifically, at paragraph 24, the specification explains that the chicoric acid concentrations measured and reported at Table I on page 6 of the specification represent variations in chicoric acid levels that generally are accepted by those skilled in the art. Thus, the values reported at Table I are representative of the levels of chicoric acid concentrations that would be acceptable to one of ordinary skill in the art. Applicants respectfully submit that this ground of rejection is overcome and respectfully request that it be withdrawn.

**35 U.S.C. § 103**

Claims 1, 3, 5-7 and 24 stand rejected under 35 U.S.C. § 103 as allegedly obvious in view of Seidler-Lozykowska *et al.* or Dou *et al.* in combination with Ringer *et al.*

Specifically, the Office action alleges that "one of ordinary skill in the art would have been motivated to test Echinacea products for chicoric acid content, as well as immunostiumlatory activity, because each of these were already known in the art to be desirable characteristics of Echinacea." Page 5 of the Office action mailed 12/14/06.

Applicants respectfully disagree that claims 1, 3, 5-7, and 24 are obvious in view of Seidler-Lozykowska *et al.* or Dou *et al.* in combination with Rininger *et al.* To render the claims obvious, three basic criteria must be met by either the references themselves or the knowledge in the art. *See* MPEP § 2143. First, there must be some suggestion or motivation to combine the references to reach the claimed invention. Second, there must be a reasonable expectation that combining the references will successfully arrive at the claimed invention. Third, when combined, the references must teach all elements of the claimed invention.

In this case, the Office action alleges that the first criteria is satisfied because the "desirable characteristics" of *Echinacea* disclosed in each of the cited references would motivate or suggest to one of skill in the art to combine the teachings of those references. However, simply because two characteristics of a plant may be desirable does not necessarily mean that those of skill in the art would seek to combine those characteristics, particularly when the art teaches against such a combination. The art references relied on in the Office action clearly do not suggest or motivate one of skill in the art to combine any characteristics of *Echinacea,* and as described below, the cited references specifically teach against the possibility of combining the characteristics of (1) standardization of an *Echinacea* extract to a particular polyphenol or phenolic acid level and (2) maximization of the immunostimulatory activity of an *Echinacea* extract. This is significant because as written, the claims are directed to a method for determining optimal harvest window of *Echinacea* plants that are to be used to prepare a standardized *Echinacea* extract by selecting the maturation stage that has <u>both</u> a concentration of a marker compound, such as chicoric acid, that is acceptable for standardization, and the highest level of immune-stimulatory product.

There is nothing in the cited references motivating or suggesting to one of ordinary skill in the art that they should be combined to arrive at the claimed invention. Specifically, both Dou and Seidler-Lozykowska examine when the greatest levels of typical marker compounds (*i.e.* polyphenolics, phenolic acids such as chicoric acid, caffeic acid, *etc.*) used to standardize extracts may be obtained and from which specific parts of the plant they may be obtained. For example, Seidler-Lozykowska explains that the purpose of their study was to aid in standardization of *Echinacea* supplements by identifying stages of *Echinacea* plant development having uniformity of chemical standards. Seidler-Lozykowska *et al.*, "Yield and Polyphenolic Acids Content in Purple Coneflower (*Echinacea purpurea* Moench.) at Different Growth Stages." 2003, *J. Herbs, Spices & Medicinal Plants,* 10(3):7-12, 11. Thus, Seilder-Lozykowska *et al* concluded that their finding that "[t]he content of polyphenolic acids was highest in leaf blades . . . in almost all stages of plant development," supports their conclusion that leafy cultivars should be bred in Poland's *Echinacea* breeding program. Seidler-Lozykowska, pages 9 and 11. Seidler-Lozykowska also teaches that polyphenolics are highest during the full flower stage of development. Dou simply looked at when it was possible to achieve the highest levels of chicoric acid, a common chemical standard for *Echinacea.* Dou concluded that chicoric acid is highest in the overground part of *Echinacea* before and after the bloomy stage. Significantly, neither Dou nor Seilder-Lozykowska suggest looking for references that discuss the immunostimulatory activity of *Echinacea,* or suggest that a harvest time might be selected based on the ability to increase the immuno-stimulatory activity of an *Echinacea* extract.

Rininger is directed at determining immunostimulatory activity of various *Echinacea* extracts. Significantly, Rininger teaches that "[f]inished products and raw materials comprised of *Echinacea* extracts that have been standardized to contain 4% phenolic compounds such as . . . chicoric acid . . . were inactive for induction of macrophage cytokine production." Rininger *et al.*, "Immunopharmacological activity of *Echinacea* preparations following simulated digestion on murine macrophages and human peripheral blood mononuclear cells." *Journal of Leukocyte Biology,* 2000;68:503-510. Indeed, according to Rininger, chemically standardized *Echinacea* extracts are inactive

as immunostimulatory agents. Abstract. Further, Rininger teaches that the chemical standards commonly used to standardize *Echinace* extracts, *e.g.* chlorogenic acid, do not possess any immunostimulatory activity. Thus, Rininger teaches against using standardized *Echinacea* extracts, or the active constitutents of standardized *Echinacea* extracts, when seeking to achieve an immunostimulatory effect using an *Echinacea* extract. Moreover, one of ordinary skill in the art would understand, based on the teachings of Rininger, that standardized *Echinacea* extracts do not exhibit immunostimulatory properties. This teaching makes it improper to combine the Rininger reference with any reference directed at maximizing a chemical standard that is used in standardizing the extract. Specifically, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983) (The claimed catalyst which contained both iron and an alkali metal was not suggested by the combination of a reference which taught the interchangeability of antimony and alkali metal with the same beneficial result, combined with a reference expressly excluding antimony from, and adding iron to, a catalyst.).

Moreover, even if it were proper to combine either Dou or Seidler-Lozykowska *et al* with Rininger, doing so would not lead one of ordinary skill in the art to have a reasonable expectation of success. Specifically, as discussed above, the claims are directed to a method for determining optimal harvest window of *Echinacea* plants that are to be used to prepare a standardized *Echinacea* extract by selecting the maturation stage that has *both* a concentration of a marker compound, such as chicoric acid, that is acceptable for standardization, and the highest level of immune-stimulatory product. One of the references relied on in the combination explicitly teaches that standardized *Echinacea* extracts do not possess immuno-stimulatory activity. Therefore, one of ordinary skill in the art would not have a reasonable expectation of success at using the claimed method, which involves a step of selecting the maturation stage that has both a concentration of marker compound acceptable for standardization, and the highest level of immune-stimulatory product.

Finally, the combined references do not teach or suggest all of the claim limitations. Specifically, the combined references do not teach a step of selecting a plant maturation stage based on the plant having both a concentration of a marker compound that is acceptable for standardization and the highest level of immune-stimulatory product.

Thus, the Office action fails to establish that claims 1, 3, 5-7, and 23-25 are obviousness in view of the cited references. Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

**SUMMARY**

Applicants believe that currently pending claims 1, 3, 5-7, and 23-25 are patentable. The Examiner is invited to contact the undersigned attorney for Applicants via telephone if such communication would expedite allowance of this application.

Respectfully submitted,

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